Quick guide

Cajal-Retzius cells

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What is a Cajal-Retzius cell? A transient class of neurons found in the surface of the developing cerebral cortex of mammals. They are named after Santiago Ramón y Cajal and Gustaf Retzius, who first described them at the end of the 19th century. These 'special cells', as Cajal initially called them, populate the marginal zone of the cortex from early stages of development (Figure 1), and thus have a strategic position to influence its organization. Cajal-Retzius cells have a peculiar morphology with distinctive horizontal dendrites, and they release the neurotransmitter glutamate. Most Cajal-Retzius cells are eliminated through cell death during early postnatal stages.

Why are they important? In contrast to most neurons, Cajal-Retzius cells are not known for their role in information processing, but rather for their job as 'project managers' in the construction of the cerebral cortex. They influence the organization of the developing cortex by releasing signals that affect the underlying neurons. One of these signals is Reelin, an extracellular glycoprotein that is required for the normal lamination of the cerebral cortex. The absence of Reelin or other molecules from its signaling pathway result in a severe disruption of the laminar organization of the cortex.

Where do they come from? Although it was initially thought that Cajal-Retzius cells originate from precursor cells throughout the cortex, they actually emerge from focal sources located at the borders of the developing pallium (a more general name for the cortex). The main source of Cajal-Retzius cells is the cortical hem, which is located in the caudomedial region of the pallium, close to the hippocampal primordium. Other sources of Cajal-Retzius cells are the pallial septum and the ventral pallium. The simultaneous production of Cajal-Retzius cells at several sites may guarantee a complete coverage of all regions of the cerebral cortex.

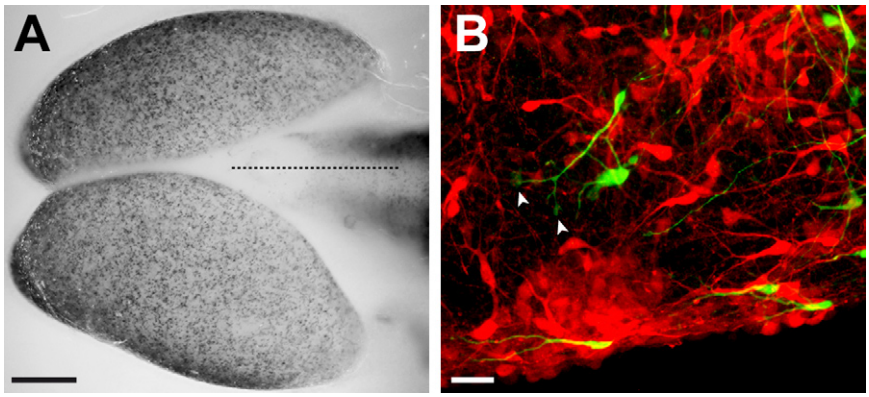

Figure 1. Distribution and morphology of Cajal-Retzius cells during embryonic development. (A) Cajal-Retzius cells — identified here by the expression of Reelin mRNA — populate the entire surface of the developing cortex in this dorsal view of a E12.5 mouse brain. The dotted line indicates the midline, rostral is to the left. (B) A detail of the cortical marginal zone, through which Cajal-Retzius cells migrate (in red, stained with antibodies against the calcium binding protein Calretinin). Some Cajal-Retzius cells also express GFP in this image. The arrowheads point to growth cones tipping the leading process. Scale bars equal 200 μm (A) and 50 μm (B).

Are all Cajal-Retzius cells equal? Cajal-Retzius cells generated at different sites differ in their neurochemical content, which suggests that different classes of Cajal-Retzius cells may exist. As a result, the relative contributions of each source to the complement of Cajal-Retzius cells vary in different cortical areas. In other words, even though Cajal-Retzius cells end up homogenously distributed throughout the entire cortex, each cortical area contains a different proportion of different types of Cajal-Retzius cells. This observation has led to the hypothesis that signals released from distinct classes of Cajal-Retzius cells may affect cortical patterning.

How do they reach their final position? Because they are born at restricted locations, Cajal-Retzius cells must disperse tangentially to cover the entire cortical surface (Figure 1). The migration of Cajal-Retzius cells seems to be highly dependent of the meninges, the system of membranes that envelopes the brain. They release signals (e.g. chemokines) that promote the movement of Cajal-Retzius cells close to the surface of the cortex.

What happens if Cajal-Retzius cells screw up? As might be expected from their job in building the cortex, abnormal generation of Cajal-Retzius cells or disruption of the expression of Reelin has catastrophic effects: the laminar organization of the neocortex and the hippocampus gets completely messed up, even though neurons are generated in normal numbers. In humans, decreased Reelin has been associated with lissencephaly, autism, schizophrenia and bipolar disorder.

Are Cajal-Retzius cells unique to mammals? Cajal-Retzius cells seem to be present in reptiles and birds, although they are relatively sparse compared to mammals. This may be why non-mammalian vertebrates are mostly devoid of cortical (laminar) structures in the telencephalon. The number and morphological intricacy of Cajal-Retzius cells increase in parallel to the complexity of the neocortex, which is highly expanded in mammals and reaches its peak in humans.

Where can I find out more?

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